# To study different etiological and prognostic factors in patients suffering from ARDS/ALI

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#### Abstract

**Background:** Acute inflammatory reaction in the lung which causes injury to the endothelial cells and alveolar epithelium are main pathological changes that may occur in ARDS. This leads to pulmonary edema which eventually causes respiratory failure in these patients. Multiple organ dysfunction syndrome (MODS) is common consequence in these patients. Mortality rate corresponds to the severity of underlying disease and it ranges from 10% to 90%.

**Methodology:** All patients were screened for the diagnostic criteria of ARDS as per the 1994 American European Consensus Conference on ARDS/ALI. Different scores suggesting outcome were calculated on admission to intensive care unit. Objectives of study were [1] To identify the different risk factors responsible for ARDS/ALI, [2] To study the lung functions in ARDS/ALI survivors, [3] To analyze the effect of treatment strategies on lung functions in survivor, [4] To study different scoring systems.

**Results:** In our study we had a total of 65 patient, out of which 35 survived. The risk factors for developing ALI/ARDS were pneumonia, tropical diseases, postoperative sepsis, poly trauma, tuberculosis, malignancy, poisoning and neurological disorder.

**Conclusions:** Pneumonia and tropical diseases are the common risk factor for the ARDS/ALI. The presence of co-morbid conditions also affects the outcome of ALI/ARDS patients. MODS of >4, LIs >2 and APACHE II >2 had associated with higher mortality.

Keywords: ARDS; ALI; Pneumonia.

#### Introduction

Acute respiratory distress syndrome (ARDS) is common outcome in patients with critical underlying diseases. Acute inflammatory reaction in the lung which causes injury to the endothelial cells and alveolar epithelium are main pathological changes that may occur in ARDS. This leads to pulmonary edema which eventually causes respiratory failure in these patients [1]. Disease with lesser severity is known as acute lung injury (ALI). In ARDS there is increased micro vascular permeability localized to the lung secondary to generalized inflammatory disorder termed as systemic inflammatory response disorder (SIRS) [2-4]. Although an increase in vascular permeability and subsequent interstitial and air space edema are initially major consequences of the acute inflammatory response, the injury involves severe damage to endothelial cells in multiple organs especially in the setting of sepsis and trauma. If the patient survives the consequences of pulmonary edema, manifestations of other systems dysfunction soon appear resulting in multi organ dysfunction syndrome (MODS) [4,5].

Sepsis, gastric aspiration, lung contusion, massive transfusion of blood, pneumonia, and major trauma are the common causes of ARDS/ALI [6]. Several attempts made to define ARDS/ALI which would be useful in clinical management [7]. Different scoring systems have been devised for determining outcome and planning further management. The newer modalities of treatment that aim at providing improving gas exchange and preventing structural lung injury due to the ventilator are commonly used. These include the use low tidal volumes, the application of high levels of positive end-expiratory pressure (PEEP), permissive hyper apnea, cyclic prone positioning and nitric oxide inhalation. Other measures include surfactant therapy, liquid ventilation, extra corporeal membrane oxygenation (ECMO).

All these treatment modalities aim at not only to reduce the mortality but also the long-term effects of mechanical ventilation in survivors. Some of the survivors have persistent impairment because of ventilator defects, bronchial hyper reactivity, impaired diffusing capacity of the lung for carbon monoxide (DLCO), and a drop in Pa02 during exercise. The mortality rates of ARDS/ALI are generally reported to exceed 50% and range from 10 to 90% depending on the etiology, severity, definition of ALI/ARDS, and the presence of pre-existing disease [8-11]. So this study was planned to find out the factors affecting or predict the outcome of disease and to evaluate different treatment modalities in the management of patients with ARDS/ALI.

### Materials and Methods

This was a prospective cohort (analytical epidemiology) study conducted in compliance with the protocol, after Institutional Ethics Committee (IEC) approval, informed consent regulations, as per Declaration of Helsinki and the ICMR guidelines for Biomedical Research on Human Subjects. All the survived cases of ARDS/ALI attending tertiary health care center in the year of 2008 were enroll in the study. All patients were screened for the diagnostic criteria of ARDS according to American European consensus definition (1994). Patients with diagnosis of ARDS/ALI having age more than 12 years and willing to take part in the study and given consent were recruited. Patients having contraindication for Pulmonary function test, history of recent myocardial infarction and active hemoptysis were excluded from the study. All patients willing to participate and give an informed consent were screened for eligibility. Baseline evaluation included recording of demographic details, medical history, general and systemic examination, and laboratory investigations, which included complete

haemogram, PFT (using Jaeger PFT machine), DLCO and chest X-ray. Further investigations included a peripheral smear for malarial parasite and tri-dot test for leptospirosis. A coagulation profile including levels of APTT (Activated Partial Thromboplastic time) and PT (prothrombin Time) was recorded. The severity of the illness was measured by the Acute Physiology and Chronic Health Evaluation (APACHE) Scrore [12], Multiple Organ Dysfunction score [13] (MODS) lung injury score (LIS) and Sequential Organ Dysfunction Assessment [14] (SOFA score). These scores were calculated on admission to our intensive care unit.

Objectives of study were (1) To identify the different risk factors responsible for ARDS/ALI. (2) To study the lung functions in ARDS/ALI survivors. (3) To analyze the effect of treatment strategies on lung functions in Survivor. (4) To study different scoring systems, MODS (Multiple Organ Dysfunction Score), SOFA (Sequential Organ Function Assessment), LIS (Lung Injury Severity) and APACE II (Acute Physiological, age and Chronic Health Evaluation II) in ALI/ARDS.

### Results

In our study we had a total of 65 patient, out of which 35 survived. We had a mortally rate of 46.2%. The mean age of the patients in our study was 33.37 ( $\pm$ 15.14) years in survivors and 39.40 ( $\pm$ 15.49) years in the non-survivors. The risk factors for developing ALI/ARDS were pneumonia (21 patients), tropical diseases (15 patients), postoperative sepsis (8 patients), poly trauma (8 patients), tuberculosis (6 patients), malignancy (3 patients), poisoning (2 patients) and neurological disorder (2 patients).

## Discussion

The ARDS is a disease with a high mortality and is a common cause of admission into intensive care units (ICUs) all over the world [15-18]. The American-European Consensus Conference definition of ALI and ARDS was published in 1994. This definition is simple to apply in the clinical setting and also recognizes that the severity of clinical lung injury varies according to the severity of arterial hypoxemia [19].

The risk factors for developing ALI/ARDS in our study were Pneumonia (32.3%), Tropical diseases (23.07%), Postoperative sepsis (12.3%), Poly trauma (12.3%), Tuberculosis (9.2%), Malignancy (4.6%), Poisoning (3.1%) and Neurological disorder (3.1%). In the study by Vigg et al., [20] the common risk factors for ALI/ARDS were pneumonia (30%), recent surgery in abdomen (10%), septicemia with MOF (18%), and trauma (12%). Other significant causes were pancreatitis, thermal burns> 40% (6%), peritonitis, falciparum malaria and poisoning. Similar findings were also find in the studies by Zilberberg et al., [21]. When compared with the risk factor associated with the non-survivors in our study, it is observed that the most common risk factor is pneumonia and that the incidence of sepsis, poly trauma is quite similar in both the studies however the incidence of tropical diseases is much higher in our study.

The presence of co-morbid conditions also affects the outcome of ALI/ARDS patients. In our study 15% of the

patients had respiratory diseases, 7.7% of the patients had hypertension, 6.2% of the patients had diabetes mellitus, 3% of the patients had HIV and 1.5% of the patients had ischemic heart disease. It was observed that 18.5% of the patients used to consume alcohol. However none of the above factors affected the outcome of the patients significantly. In the study by Silberberg et al., [21] it was observed that cirrhosis of the liver (20%), HIV infection (10%), active malignancy (24%) and organ transplantation (9%) were the common co-morbid conditions in the patients dying due to ALI/ARDS. In the study by Vigg et al., [20] 20% of the patients had hypertension, 8% of the patients had diabetes mellitus and 3% of the patients had coronary artery disease. The low incidence of the co-morbid conditions like malignancy, HIV infection in our study could represent a lack of awareness and early detection of these conditions in the general population.

An attempt was made to analyze the presenting clinical features of the patient and the impact they had on the outcome. It was observed that most of the patients presented within 10 days of the onset of the symptoms. Dyspnea was present in almost all cases. Fever was seen in majority of patients with duration of 2 to 4 days. History of wading through water was present in 27(73%) cases, this can be attributed to the similar frequency of leptospirosis 22(59.5%) which is water borne infection. 11(29.7%) patients had history of hemoptysis. Duration of cough related with the outcome of disease. Prognosis was better in patients with duration of cough less than 10 days. Hence early detection of symptoms like cough could alter the outcome of the disease.

Systemic abnormalities were found in majority of cases in the form of hematological, renal and liver dysfunction. These finding in our study show similar pattern as in the study carried out by Zilberberg et al., [21]. In a study by Fallow et al., [22] renal and Hematological dysfunction have been shown to be independent predictors of mortality. The organisms that were commonly isolated in cultures (blood and sputum) were pseudomonas and Klebsiella. A similar organism's pattern was seen in patient's studies by Vigg et al., [20].

A number of studies had found a direct association between poor oxygenation and mortality whereas other studies have failed to identify a correlation [23-26]. When tested prospectively, increasing severity of lung injury (using LIS Score), measured at 24, 48, and 72 hours, wasn't associated with increased mortality [26]. We also observed that a MODS of >4, LIs >2 and APACHE II >2 had higher association with mortality. The mean score in non-survivors were as follows: MODS 5.3, LIS 2.3 and APACHE II 17.6 these scoring systems were equally effective in predicting mortality in ALI/ARDS due to tropical diseases. The SOFA score was not found to be useful in predicting the outcome. It should be noted that we had used the scores only during assessment of the patients on the first day of admission in our ICU. The mean P/F ratio was 208 in survivors and 167 in nonsurvivors in our study. However no significant difference has been found in the P/F ratio in survivors and non-survivors in other studies [21,26].

In our study 60% of the patients required mechanical ventilation. The patients were ventilated using ACMV (Assist control mechanical ventilation) or control mode and a lung protective strategy with tidal volume of 8ml/kg was given with PEEP whenever required. Inverse ratio ventilation and prone pressure ventilation were also attempted in a few cases. The significant finding was that survivors spent lesser number of days (mean 2.74 days) on ventilator than non-survivors (mean 8.73 days). Also 50% of the deaths were within the first 24 hours. In the study by Vigg et al., [20] duration of ventilation was less than 7 days in 80% of the patients (dead) while the same was 66% in non-survivors in our study and 71% in survivors. The use of steroids in our study did not reduce the mortality as in other studies [27,28]. In the survivors a PFT was done in 34% of the patients. It was

seen that overall 43% has an obstructive and restrictive pattern 28.5% had an obstructive pattern and 28.5% had a normal PFT. It was also seen that none of these patients had preexisting respiratory disease. Mean pO2 on discharge was 81 mm of Hg so a long-term prospective trial is essential to look at the long-term effects of ALI/ARDS patients in the survivors of this condition.

#### Conclusions

Pneumonia and tropical diseases are the common risk factor for the ARDS/ALI. The presence of co-morbid conditions also affects the outcome of ALI/ARDS patients. MODS of >4, LIs >2 and APACHE II >2 had associated with higher mortality.

Table 1	: Demographic and	clinical details of	patients with ARDS/ALI	(both survivors and non survivors)
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Parameter		Alive	Dead	
		Patients	Patients	
		In numbers	In numbers	
Age (in years)	<25	14	4	
	25-60	17	23	
	>60	4	3	
Sex	Male	21	23	
	Female	14	7	
Diagnosis	Pneumonia	12	9	
	Post-operative sepsis	4	4	
	Poly trauma	4	4	
	Carcinoma	0	3	
	Neurological Disorder	1	1	
	TB	6	0	
	Poisoning	1	1	
	Tropical diseases	7	8	
	Sub groups in tropical diseases			
	Leptospirosis	3	3	
	Malaria	2	0	
	Dengue	1	0	
	Malaria + Leptospirosis	1	0	
	Undiagnosed	0	5	
Time since onset	<10days	24	19	
	>10days	11	11	
Fever	No	7	2	
	<8days	28	28	
Cough	No	10	8	
	<8days	21	9	
	>8days	4	13	
Breathlessness	No	3	6	
	<8days	24	14	
	>8days	8	10	
Bleeding	Yes	4	4	
	No	30	26	
	Epistaxis	1	0	
Tuberculosis	Yes	3	0	
	No	32	30	
Ischemic heart disease	Yes	1	2	
	No	34	27	

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Respiratory disease	COPD	1	0
	Byssinosis	1	1
	Bronchiectasis	1	3
	Bulla	0	1
	Nil	32	0
Hypertension	Yes	2	3
	No	33	28
diabetes mellitus	Yes	2	2
	No	33	22
Smoker	Yes	6	8
	No	29	23
Alcoholic	Yes	5	7
	No	30	11
Temperature <sup>o</sup> C		37.20	37.09
Pulse (/min)		108	116
Respiratory rate (/min)		34	38
Glasgow coma scale		13	12
Pallor	Yes	15	5
	No	20	25
Cyanosis	Yes	3	27
	No	32	3
Skin Rash	Yes	35	27
	No	0	3
Platelets in lacks		2.1	1.6
PT/APTT	Normal	1	13
	Deranged	34	17
DIC	Yes	8	11
	No	27	19
Liver dysfunction	Absent	11	16
	Present	24	14
Renal dysfunction	Absent	14	11
	Present	21	19
P/F ratio		208	167
SOFA	<5	19	11
	>5	16	19
MODS	<4	21	8
	>4	14	22
LIS	<2	14	5
	>2	21	25
APACHE II	<12	19	6
	>12	16	24
Steroids taken	Yes	3	6
	No	32	24
Days on ventilator		3	9

APTT: Activated Partial Thromboplastic time; PT: disseminated intravascular prothrombin Time; DIC: coagulation; P/F: SOFA Score: Sequential Organ Dysfunction Assessment; MODS: Multiple Organ Dysfunction score; LIS: lung injury score; APACHE: Acute Physiology and Chronic Health Evaluation.

Conflicts of Interest: None declared.

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